USPAT2
NEWS 5 JAN 13 IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS 6 JAN 13 New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS 7 JAN 17 Pre-1988 INPI data added to MARPAT
NEWS 8 JAN 17 IPC 8 in the WPI family of databases including WPIFV
NEWS 9 JAN 30 Saved answer limit increased
NEWS 10 JAN 31 Monthly current-awareness alert (SDI) frequency added to TULSA
NEWS 11 FEB 21 STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS 12 FEB 22 Status of current WO (PCT) information on STN
NEWS 13 FEB 22 The IPC thesaurus added to additional patent databases on STN
NEWS 14 FEB 22 Updates in EPFULL; IPC 8 enhancements added
NEWS 15 FEB 27 New STN AnaVist pricing effective March 1, 2006
NEWS 16 FEB 28 MEDLINE/LMEDLINE reload improves functionality
NEWS 17 FEB 28 TOXCENTER reloaded with enhancements
NEWS 18 FEB 28 REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS 19 MAR 01 INSPEC reloaded and enhanced
NEWS 20 MAR 03 Updates in PATDPA; addition of IPC 8 data without attributes
NEWS 21 MAR 08 X.25 communication option no longer available after June 2006
NEWS 22 MAR 22 EMBASE is now updated on a daily basis
NEWS 23 APR 03 New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS 24 APR 03 Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL
NEWS 25 APR 04 STN AnaVist $500 visualization usage credit offered

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005. V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT http://download.cas.org/express/v8.0-Discover/

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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:03:33 ON 05 APR 2006

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.42	0.42

FILE 'REGISTRY' ENTERED AT 13:04:29 ON 05 APR 2006
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 4 APR 2006 HIGHEST RN 879269-14-4
DICTIONARY FILE UPDATES: 4 APR 2006 HIGHEST RN 879269-14-4

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TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

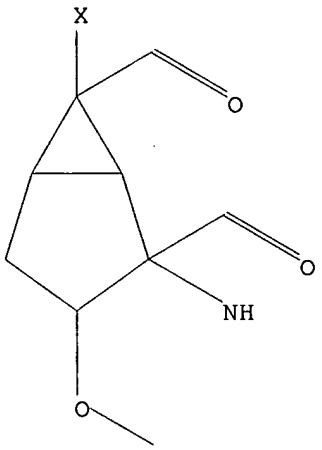
****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

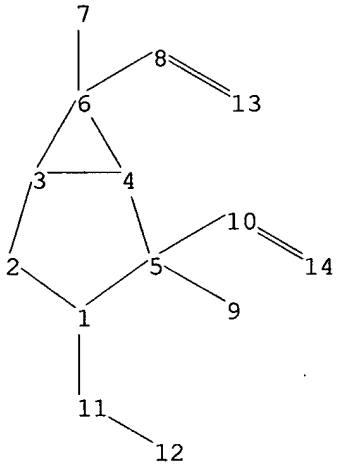
Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Documents and Settings\PZucker\My Documents\Examination Auxillary files\10500101\10500101 clm 2 core obv.str



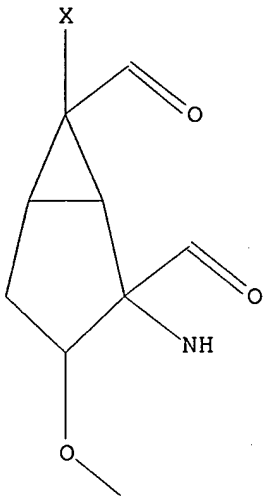


chain nodes :
7 8 9 10 11 12 13 14
ring nodes :
1 2 3 4 5 6
chain bonds :
1-11 5-9 5-10 6-7 6-8 8-13 10-14 11-12
ring bonds :
1-2 1-5 2-3 3-4 3-6 4-5 4-6
exact/norm bonds :
1-2 1-5 1-11 2-3 3-4 3-6 4-5 4-6 5-9 8-13 10-14 11-12
exact bonds :
5-10 6-7 6-8

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> search l1 sss sam
SAMPLE SEARCH INITIATED 13:04:55 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 11 TO ITERATE

100.0% PROCESSED 11 ITERATIONS 9 ANSWERS
SEARCH TIME: 00.00.01

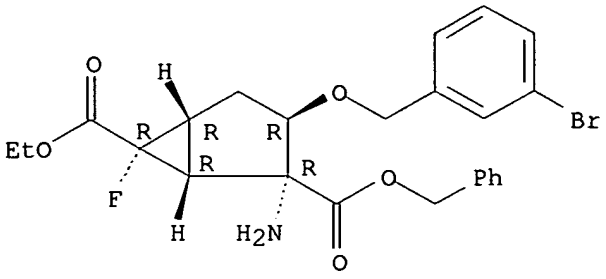
FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 22 TO 418
PROJECTED ANSWERS: 9 TO 360

L2 9 SEA SSS SAM L1

=> d scan

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-bromophenyl)methoxy]-6-fluoro-, 6-ethyl 2-(phenylmethyl) ester, (1R,2R,3R,5R,6R)- (9CI)
MF C24 H25 Br F N O5
CI COM

Absolute stereochemistry.

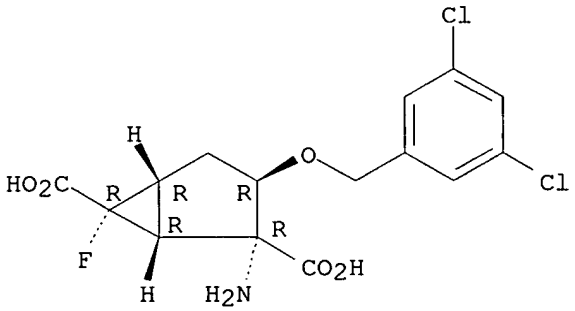


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):3

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,5-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI)
MF C15 H14 Cl2 F N O5

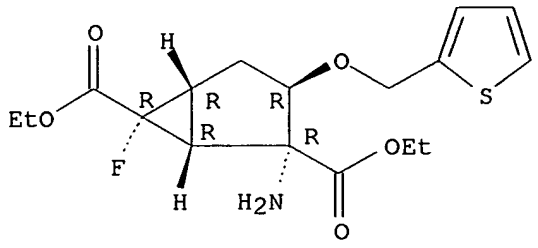
Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-(2-thienylmethoxy)-, diethyl ester, (1R,2R,3R,5R,6R)- (9CI)
MF C17 H22 F N O5 S
CI COM

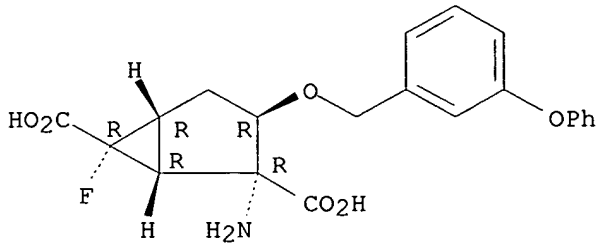
Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3-phenoxyphenyl)methoxy]-, (1R,2R,3R,5R,6R)- (9CI)
MF C21 H20 F N O6

Absolute stereochemistry. Rotation (-).

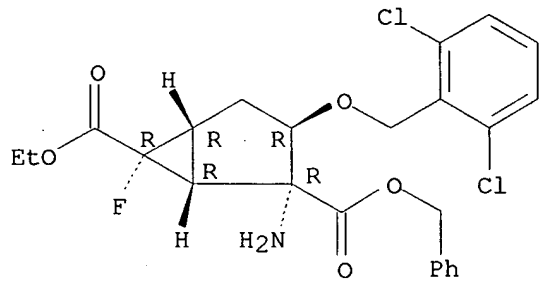


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):9

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,6-dichlorophenyl)methoxy]-6-fluoro-, 6-ethyl 2-(phenylmethyl) ester, (1R,2R,3R,5R,6R)- (9CI)
MF C24 H24 Cl2 F N O5

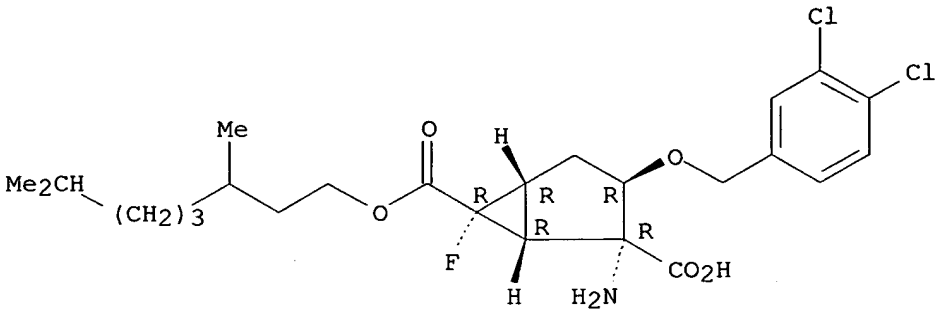
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, 6-(3,7-dimethyloctyl) ester, (1R,2R,3R,5R,6R)- (9CI)
MF C25 H34 Cl2 F N O5

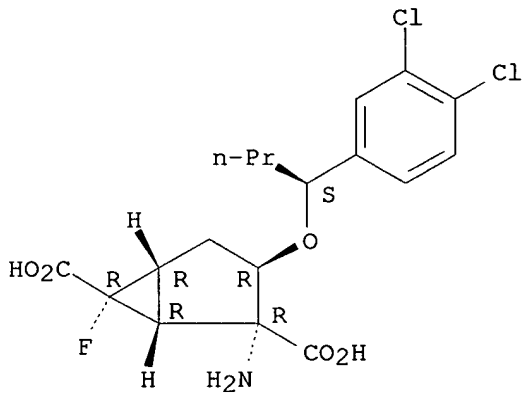
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(1S)-1-(3,4-dichlorophenyl)butoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI)
MF C18 H20 Cl2 F N O5

Absolute stereochemistry. Rotation (+).

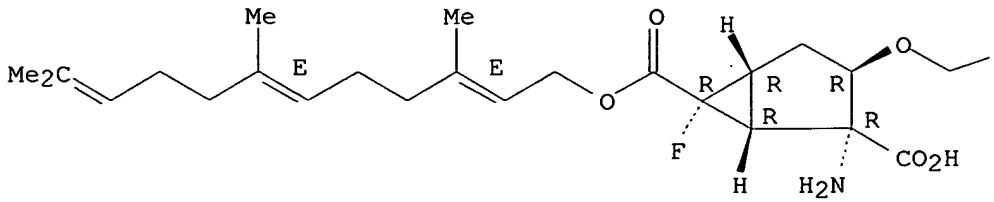


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

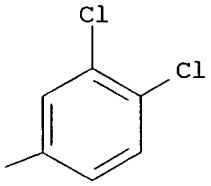
L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, 6-[(2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrienyl] ester, (1R,2R,3R,5R,6R)- (9CI)
MF C30 H38 Cl2 F N O5

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



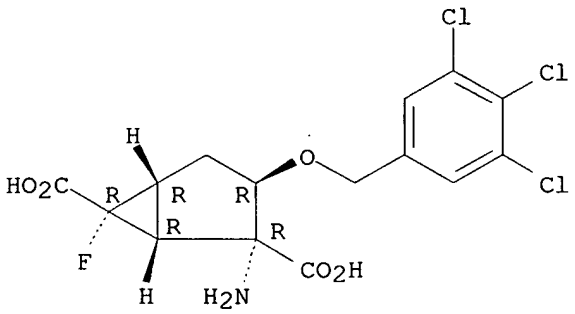
PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3,4,5-trichlorophenyl)methoxy]-, (1R,2R,3R,5R,6R)- (9CI)
MF C15 H13 Cl3 F N O5

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> search l1 sss full
FULL SEARCH INITIATED 13:06:18 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 273 TO ITERATE

100.0% PROCESSED 273 ITERATIONS 224 ANSWERS
SEARCH TIME: 00.00.01

L3 224 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY 167.82 TOTAL SESSION 168.24

FULL ESTIMATED COST

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FILE COVERS 1907 - 5 Apr 2006 VOL 144 ISS 15
FILE LAST UPDATED: 4 Apr 2006 (20060404/ED)

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=> l3
L4 11 L3

=> d l4 1-11 ti

L4 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI A metabotropic glutamate 2/3 receptor antagonist, MGS0039, increases extracellular dopamine levels in the nucleus accumbens shell

L4 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI AMPA receptor stimulation mediates the antidepressant-like effect of a group II metabotropic glutamate receptor antagonist

L4 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Neuropharmacological profiles of antagonists of group II metabotropic glutamate receptors

L4 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid esters as Group II metabotropic glutamate receptor antagonists

L4 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as antagonists of group II metabotropic glutamate receptor

L4 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI mGluR2 antagonists and 2-amino-3-alkoxy-6-[3.1.0]hexan-2,6-dicarboxylate derivatives for treatment of nervous system diseases

L4 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Anxiolytic-like activity of MGS0039, a potent group II metabotropic

glutamate receptor antagonist, in a marble-burying behavior test

L4 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Synthesis, in vitro pharmacology, structure-activity relationships, and pharmacokinetics of 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as potent and selective group II metabotropic glutamate receptor antagonists

L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI MGS0039: a potent and selective group II metabotropic glutamate receptor antagonist with antidepressant-like activity

L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Increased cell proliferation in the adult mouse hippocampus following chronic administration of group II metabotropic glutamate receptor antagonist, MGS0039

L4 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI 6-Fluorobicyclo[3.1.0]hexane derivatives

=> d l4 1-11 ti fbib abs

L4 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI A metabotropic glutamate 2/3 receptor antagonist, MGS0039, increases extracellular dopamine levels in the nucleus accumbens shell
AN 2005:1351480 CAPLUS
DN 144:81056
TI A metabotropic glutamate 2/3 receptor antagonist, MGS0039, increases extracellular dopamine levels in the nucleus accumbens shell
AU Karasawa, Jun-ichi; Yoshimizu, Takao; Chaki, Shigeyuki
CS Medicinal Pharmacology Laboratory, Medicinal Research Laboratories, Taisho Pharmaceutical Co., Ltd., Kita-ku, Saitama, 331-9530, Japan
SO Neuroscience Letters (2006), 393(2-3), 127-130
CODEN: NELED5; ISSN: 0304-3940
PB Elsevier Ltd.
DT Journal
LA English
AB MGS0039, a potent and selective metabotropic glutamate 2/3 (mGlu 2/3) receptor antagonist, exhibits antidepressant-like activities in some animal models. In the present study, the authors examined the effect of MGS0039 on extracellular dopamine levels in the rat nucleus accumbens (NAc) shell using in vivo microdialysis evaluation because accumbal dopamine has been implicated in depression. Local application of MGS0039 into the NAc shell at 10 μM significantly increased extracellular dopamine levels in the NAc shell in freely moving rats. In contrast, local application of 10 μM of LY354740, an mGlu 2/3 receptor agonist, significantly decreased extracellular dopamine levels in the same brain region. These findings suggest that dopamine release in the NAc shell is regulated by mGlu 2/3 receptors, and that the effect on dopamine levels in the NAc shell may partially explain the antidepressant-like properties of mGlu 2/3 receptor antagonists.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI AMPA receptor stimulation mediates the antidepressant-like effect of a group II metabotropic glutamate receptor antagonist
AN 2005:298938 CAPLUS
DN 142:423678
TI AMPA receptor stimulation mediates the antidepressant-like effect of a group II metabotropic glutamate receptor antagonist
AU Karasawa, Jun-Ichi; Shimazaki, Toshiharu; Kawashima, Naoya; Chaki,

Shigeyuki
CS Medicinal Pharmacology Laboratory, Medicinal Research Laboratories, Taisho Pharmaceutical Co., Ltd., Saitama, 331-9530, Japan
SO Brain Research (2005), 1042(1), 92-98
CODEN: BRREAP; ISSN: 0006-8993
PB Elsevier B.V.
DT Journal
LA English
AB (1R,2R,3R,5R,6R)-2-Amino-3-(3,4-dichlorobenzyloxy)-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid (MGS0039), a selective group II metabotropic glutamate receptor (mGluR) antagonist, exhibits antidepressant-like activities in rodent models. In the present studies, to clarify the involvement of α-amino-3-hydroxy-5-methylisoxazole-4-propionate (AMPA) receptor activation in exhibition of the antidepressant-like properties of MGS0039, the authors examined the effect of an AMPA receptor antagonist, 2,3-dihydroxy-6-nitro-7-sulfamoylbenzo(f)quinoxaline (NBQX), on the antidepressant-like effect of MGS0039 in the mouse tail suspension test. The authors also examined the effects of NBQX on increased serotonin release after treatment with MGS0039 in the rat medial prefrontal cortex (mPFC) using in vivo microdialysis evaluation. In the tail suspension test, MGS0039 (0.3-3 mg/kg, i.p.) treatment dose-dependently and significantly reduced immobility time. Pretreatment with NBQX (10 mg/kg, s.c.) significantly prevented the antidepressant-like effect of MGS0039 in the tail suspension test, while NBQX itself had no effect on immobility time. In the microdialysis evaluation, administration of MGS0039 (10 mg/kg, i.p.) significantly increased serotonin levels in mPFC in freely moving rats, while NBQX (1 mg/kg, i.p.) itself had no effect on serotonin release in this region. Pretreatment with NBQX significantly attenuated the increase in serotonin release by MGS0039. These findings suggest that stimulation of postsynaptic AMPA receptors plays a role in mediating the pharmacol. effects of MGS0039.
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Neuropharmacological profiles of antagonists of group II metabotropic glutamate receptors
AN 2005:234178 CAPLUS
DN 142:367493
TI Neuropharmacological profiles of antagonists of group II metabotropic glutamate receptors
AU Kawashima, Naoya; Karasawa, Jun-ichi; Shimazaki, Toshiharu; Chaki, Shigeyuki; Okuyama, Shigeru; Yasuhara, Akito; Nakazato, Atsuro
CS Research Strategy Group, Pharmaceutical Business Division, Taisho Pharmaceutical Co., Ltd., Saitama, Saitama, 331-9530, Japan
SO Neuroscience Letters (2005), 378(3), 131-134
CODEN: NELED5; ISSN: 0304-3940
PB Elsevier Ltd.
DT Journal
LA English
AB Glutamatergic abnormalities play roles in several psychiatric disorders. Glutamate acts at two classes of receptors, ionotropic and metabotropic glutamate receptors (mGluR), the latter is classified into three group, based on receptor homol. and signaling mechanisms. Among them, recent pharmacol. and histochem. studies suggest that the group II mGluR (mGluR2 and mGluR3) plays crucial roles in the control of emotional states. We previously reported that MGS0039, a selective group II mGluR antagonist, exhibited dose-dependent antidepressant-like effects in some animal models. However, the mechanism by which group II mGluR antagonists exhibit such effects is still unclear. In the present two studies, we examined neuropharmacol. effects of group II mGluR antagonists on monoaminergic neurons. In an electrophysiol. study, MGS0039

dose-dependently and significantly increased the firing rate of dorsal raphe nucleus (DRN) serotonergic neurons. LY341495, another group II mGluR antagonist, also increased DRN serotonergic neural activity significantly. Consistent with the findings of this electrophysiol. study, MGS0039 significantly increased extracellular level of serotonin in rat medial prefrontal cortex in a microdialysis study. In contrast, MGS0039 had no effect on the activity of locus coeruleus noradrenergic neurons. These findings suggest that modulation of serotonergic neuron might be, at least in part, responsible for the antidepressant-like effects of group II mGluR antagonists.

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid esters as Group II metabotropic glutamate receptor antagonists
AN 2005:14355 CAPLUS
DN 142:113634
TI Preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid esters as Group II metabotropic glutamate receptor antagonists
IN Yasuhara, Akito; Sakagami, Kazunari; Ohta, Hiroshi; Nakazato, Atsuro
PA Taisho Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 144 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

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	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
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				WO 2004-JP9398	W	20040625
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				WO 2004-JP9398	W	20040625
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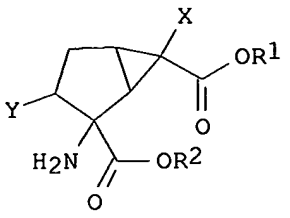
				JP 2003-373511	A	20031031
				JP 2004-128663	A	20040423
				WO 2004-JP9398	W	20040625

OS MARPAT 142:113634
GI



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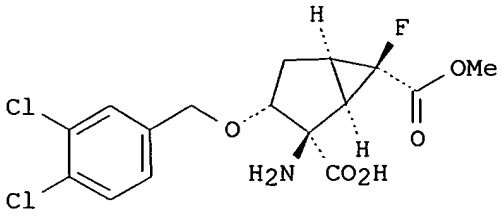


II

AB The title compds. I [wherein R1 and R2 = independently alkyl, alkenyl, alkynyl, etc.; X = H or F; Y = (un)substituted alkoxy, SH, amino, etc.] or hydrates or pharmaceutically acceptable salts thereof are prepared as Group II metabotropic glutamate receptor antagonists. For example, the compound II was prepared in a multi-step synthesis. II showed antagonistic effect on Group II metabotropic glutamate receptor in rat. I are useful for the treatment of schizophrenia, anxiety, and diseases related to these, i.e., psychiatrical disorders such as depression, bipolar disorder, and epilepsy (no data).

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

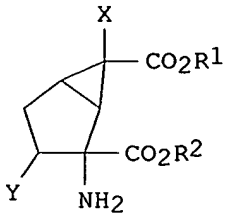
L4 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as antagonists of group II metabotropic glutamate receptor
AN 2005:14354 CAPLUS
DN 142:113754
TI Preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as antagonists of group II metabotropic glutamate receptor
IN Yasuhara, Akito; Sakagami, Kazunari; Ohta, Hiroshi; Nakazato, Atsuro
PA Taisho Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005000790	A1	20050106	WO 2004-JP9384	20040625

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

JP 2003-181931 A 20030626

OS MARPAT 142:113754
GI



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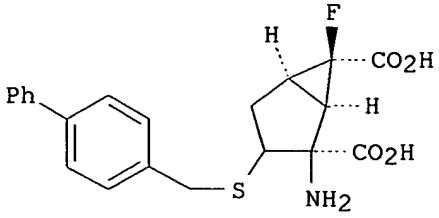


II

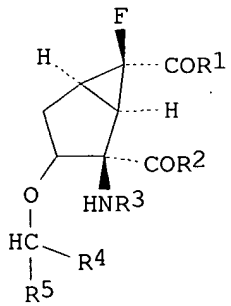
AB The title compds. [I; R1, R2 = H, C1-10 alkyl, Ph, naphthyl, mono- or diphenyl-C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, hydroxy-C2-10 alkyl, C1-10 alkoxycarbonyl-C1-10 alkyl, amino-C2-10 alkyl, C1-10 alkoxy-C1-10 alkyl; X = H, F; Y = NH2, SR3, S(O)nR7, SCHR3R4, S(O)nCHR3R4, NHCHR3R4, N(CHR3R4)(CHR5R6), NHCOR3, O2CR7; wherein R3-R6 = H, C1-10 alkyl, (un)substituted Ph, naphthyl, 1-7 halogen(s)-substituted naphthyl, heteroaryl; R7 = C1-10 alkyl, (un)substituted Ph, naphthyl, 1-7 halogen(s)-substituted naphthyl, heteroaryl; n = 1,2], pharmaceutically acceptable salts thereof, or hydrates of either are prepared These compds., e.g. (II), had an antagonistic effect on a Group II metabotropic glutamate receptor with IC50 of ≤200 nM, and are effective in treatments for and prevention of psychiatric disorders and neurol. diseases.

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI mGluR2 antagonists and 2-amino-3-alkoxy-6-[3.1.0]hexan-2,6-dicarboxylate derivatives for treatment of nervous system diseases
AN 2004:1038326 CAPLUS
DN 142:16843
TI mGluR2 antagonists and 2-amino-3-alkoxy-6-[3.1.0]hexan-2,6-dicarboxylate derivatives for treatment of nervous system diseases
IN Nakazato, Atsuro; Taki, Shigeyuki; Sakagami, Kazunari; Dean, Reiko; Ota, Hiroyuki; Hirota, Shiho; Yasuhara, Akitaka
PA Taisho Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 70 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
PI	JP 2004339199	A2	20041202	JP 2004-86153		20040324
				JP 2003-117907	A	20030423

OS MARPAT 142:16843
GI

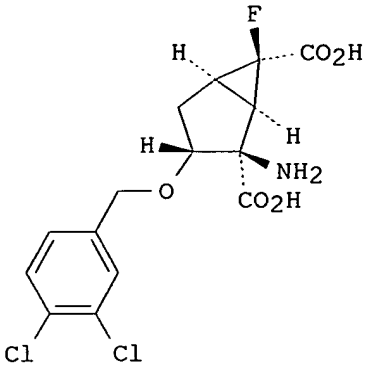


I

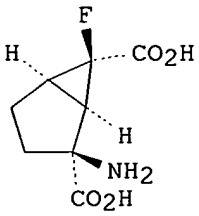
AB The antidepressant mGlur2 antagonists and 2-amino-3-alkoxy-6-[3.1.0]hexan-2,6-dicarboxylate derivs., salts, and hydrates are claimed for treatment of nervous system diseases, including bipolar affective disorder, psychiatry disorder, anxiety, epilepsy, drug dependence, cognition disorder, Alzheimer's disease, Huntington's disease, Parkinson disease, muscle stiffness, brain ischemia, spinal cord injury, head injury, etc.

L4 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Anxiolytic-like activity of MGS0039, a potent group II metabotropic glutamate receptor antagonist, in a marble-burying behavior test
AN 2004:814656 CAPLUS
DN 141:325597
TI Anxiolytic-like activity of MGS0039, a potent group II metabotropic glutamate receptor antagonist, in a marble-burying behavior test
AU Shimazaki, Toshiharu; Iijima, Michihiko; Chaki, Shigeyuki
CS Psychiatric Diseases and Pain Research, Medicinal Pharmacology Laboratory, Medicinal Research Laboratories, Taisho Pharmaceutical Co., Ltd., Saitama, Saitama, 331-9530, Japan
SO European Journal of Pharmacology (2004), 501(1-3), 121-125
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier B.V.
DT Journal
LA English
AB Glutamatergic abnormalities are involved in several psychiatric disorders. Clin. evidence demonstrates altered glutamatergic neurotransmission in patients suffering from obsessive-compulsive disorder. MGS0039, (1R,2R,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzyloxy)-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid, is a novel group II metabotropic glutamate (mGlu) receptor antagonist. We examined MGS0039's potential anti-obsessive-compulsive disorder activity, using the marble-burying behavior test as a model of obsessive-compulsive disorder. MGS0039 as well as LY341495 ((2S,1'S,2'S)-2-(9-xanthylmethyl)-2-(2'-carboxycycloprolyl)glycine), another group II mGlu receptor antagonist, inhibited marble-burying behavior. We also demonstrated that this effect was significantly attenuated by a group II mGlu receptor agonist. This data indicates that group II mGlu receptor antagonists may exert anti-obsessive-compulsive disorder effects in clin. use.
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Synthesis, in vitro pharmacology, structure-activity relationships, and pharmacokinetics of 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as potent and selective group II metabotropic glutamate receptor antagonists
AN 2004:620394 CAPLUS
DN 141:243074
TI Synthesis, in vitro pharmacology, structure-activity relationships, and pharmacokinetics of 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as potent and selective group II metabotropic glutamate receptor antagonists
AU Nakazato, Atsuro; Sakagami, Kazunari; Yasuhara, Akito; Ohta, Hiroshi; Yoshikawa, Ryoko; Itoh, Manabu; Nakamura, Masato; Chaki, Shigeyuki
CS Medicinal Chemistry Laboratory, Taisho Pharmaceutical Co. Ltd., Kita-ku, Saitama-shi, Saitama, 331-9530, Japan
SO Journal of Medicinal Chemistry (2004), 47(18), 4570-4587
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 141:243074
GI



I



II

AB Group II metabotropic glutamate receptor (mGluR) antagonists, 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivs., e.g., I, were discovered by the incorporation of a hydroxy or alkoxyl group onto the C-3 portion of selective and potent group II mGluR agonist II. Among these compds., I (MGS0039) was a highly selective and potent group II mGluR antagonist with the best pharmacokinetic profile. I exhibited high affinities for mGlu 2 (Ki = 2.38 ± 0.40 nM) and mGlu 3 (4.46 ± 0.31 nM) but low affinity for mGluR 7 (Ki = 664 ± 106 nM), and potent antagonist activities for mGlu 2 (IC50 = 20.0 ± 3.67nM) and mGluR 3 (IC50 = 24.0 ± 3.54 nM) but much less potent antagonist activities for mGlu 4 (IC50 = 1740 ± 1080 nM), mGlu 6 (IC50 = 2060 ± 1270 nM), mGlu 1 (IC50 = 93300 ± 14600 nM), and mGluR 5 (IC50 = 117000 ± 38600 nM). No significant agonist activities of I were found for mGluRs 2, 3, 4, 6, 1, and 5 (EC50 > 100000 nM). Furthermore, I exhibited dose-dependent oral absorption (plasma Cmax: 214 ± 56.7, 932 ± 235, and 2960 ± 1150 ng/mL for 3 mg/kg, 10 mg/kg, and 30 mg/kg, po, resp.) and acceptable blood-brain barrier penetration (brain Cmax: 13.2 ng/mL for 10 mg/kg, po 6 h). The synthesis, in vitro pharmacol. profile, and structure-activity relationships of 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivs., and pharmacokinetic profiles of several typical compds, are presented.

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI MGS0039: a potent and selective group II metabotropic glutamate receptor antagonist with antidepressant-like activity
AN 2004:126085 CAPLUS
DN 141:82129
TI MGS0039: a potent and selective group II metabotropic glutamate receptor antagonist with antidepressant-like activity
AU Chaki, Shigeyuki; Yoshikawa, Ryoko; Hirota, Shiho; Shimazaki, Toshiharu; Maeda, Maoko; Kawashima, Naoya; Yoshimizu, Takao; Yasuhara, Akito; Sakagami, Kazunari; Okuyama, Shigeru; Nakanishi, Shigetada; Nakazato, Atsuro
CS Medicinal Research Laboratories, Taisho Pharmaceutical Co., Ltd., Saitama, 331-9530, Japan
SO Neuropharmacology (2004), 46(4), 457-467
CODEN: NEPHBW; ISSN: 0028-3908
PB Elsevier Science B.V.
DT Journal
LA English
AB The present study describes the pharmacol. profile of (1R,2R,3R,5R,6R)-2-

Amino-3-(3,4-dichlorobenzyloxy)-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid (MGS0039), a novel group II mGluR antagonist. MGS0039 showed high affinity for both mGluR2 (Ki = 2.2 nM) and mGluR3 (Ki = 4.5 nM), which are comparable to LY341495, another group II mGluR antagonist. MGS0039 attenuated both glutamate-induced inhibition of forskolin-evoked cAMP formation in CHO cells expressing mGluR2 (IC50 = 20 nM) or mGluR3 (IC50=24 nM) and glutamate-increased [35S]GTPγS binding to mGluR2 (pA2=8.2), which means that MGS0039 acts as an antagonist. MGS0039 shifted the dose-response curve of glutamate-increased [35S]GTPγS binding rightward without altering the maximal response, and thereby indicating competitive antagonism. MGS0039 showed no significant effects on other mGluRs as well as the other receptors and transporters we studied. MGS0039 (0.3-3 mg/kg, i.p.) as well as LY341495 (0.1-3 mg/kg, i.p.) had dose-dependent antidepressant-like effects in the rat forced swim test and in the mouse tail suspension test. In contrast, MGS0039 (0.3-3 mg/kg, i.p.) had no apparent effect in the rat social interaction test and in the rat elevated plus-maze. These results indicate that MGS0039 is a potent and selective antagonist of group II mGluR, and that group II mGluR antagonists, like MGS0039, have an antidepressant-like potential in exptl. animal models.

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

TI Increased cell proliferation in the adult mouse hippocampus following chronic administration of group II metabotropic glutamate receptor antagonist, MGS0039

AN 2004:96754 CAPLUS

DN 140:368470

TI Increased cell proliferation in the adult mouse hippocampus following chronic administration of group II metabotropic glutamate receptor antagonist, MGS0039

AU Yoshimizu, Takao; Chaki, Shigeyuki

CS Medicinal Research Laboratories, Medicinal Pharmacology Laboratory, Psychiatric Diseases and Pain Research, Taisho Pharmaceutical Co., Ltd., Kita-ku, Saitama, 331-9530, Japan

SO Biochemical and Biophysical Research Communications (2004), 315(2), 493-496
CODEN: BBRCA9; ISSN: 0006-291X

PB Elsevier Science

DT Journal

LA English

AB We have previously reported that MGS0039, a novel antagonist of group II metabotropic glutamate receptors (mGluRs), exerts antidepressant-like effects in exptl. animal models. Recent studies suggest that the behavioral effects of chronic antidepressant treatment are mediated by the stimulation of neurogenesis in the hippocampus. In the present study, we examined the effects of MGS0039 on cell proliferation in the adult mouse hippocampus. MGS0039 (5 or 10 mg/kg) or fluvoxamine was administered chronically to male ICR mice over a period of 14 days. Multiple bromodeoxyuridine (BrdU) administrations were performed after the last drug injection to label dividing cells. Immunohistochem. analyses after BrdU injections revealed that chronic MGS0039 treatment enhanced BrdU-pos. cells in the dentate gyrus (.apprx.62% increase) in the same manner as chronic fluvoxamine treatment. This is the first in vivo study to demonstrate an increase in cell proliferation following a blockade of group II mGluRs. These findings raise the possibility that MGS0039 may exert antidepressant-like effects by modulating cell proliferation in the hippocampus.

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

TI 6-Fluorobicyclo[3.1.0]hexane derivatives
AN 2003:591035 CAPLUS
DN 139:143973
TI 6-Fluorobicyclo[3.1.0]hexane derivatives
IN Nakazato, Atsuro; Chaki, Shigeyuki; Sakagami, Kazunari; Dean, Ryoko; Ohta, Hiroshi; Hirota, Shiho; Yasuhara, Akito
PA Taisho Pharmaceutical Co.,ltd., Japan
SO PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003061698	A1	20030731	WO 2002-JP13693	20021226
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
				JP 2001-395797 A	20011227
	CA 2471642	AA	20030731	CA 2002-2471642	20021226
				JP 2001-395797 A	20011227
				WO 2002-JP13693 W	20021226
	EP 1459765	A1	20040922	EP 2002-793421	20021226
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
				JP 2001-395797 A	20011227
				WO 2002-JP13693 W	20021226
	BR 2002015462	A	20041130	BR 2002-15462	20021226
				JP 2001-395797 A	20011227
				WO 2002-JP13693 W	20021226
	CN 1610557	A	20050427	CN 2002-826388	20021226
				JP 2001-395797 A	20011227
	US 2005119345	A1	20050602	US 2003-500101	20021226
				JP 2001-395797 A	20011227
				WO 2002-JP13693 W	20021226
	ZA 2005002085	A	20050629	ZA 2005-2085	20021226
				JP 2001-395797 A	20011227
	ZA 2004004795	A	20050617	ZA 2004-4795	20040617
				JP 2001-395797 A	20011227

OS MARPAT 139:143973
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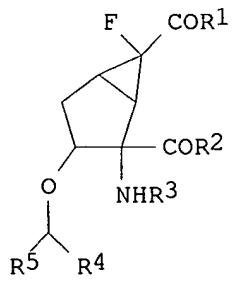

I

AB Antidepressants containing as the active ingredient compds. having group II metabotropic glutamate receptor antagonism; and 2-amino-3-alkoxy-6-fluorobicyclo[3.1.0]- hexane-2,6-dicarboxylic acid derivs. represented by the general formula [I], pharmaceutically acceptable salts thereof, or hydrates of the salts: I wherein R1 and R2 may be the same or different from each other and are each hydroxyl, C1-10 alkoxy, or the like; R3 is C1-10 acyl, C1-6 alkoxy-C1-6 acyl, or the like; and R4 and R5 may be the same or different from each other and are each hydrogen, C1-10 alkyl, or the like.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> logoff hold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	35.15	203.39

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-8.25	-8.25

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 13:08:29 ON 05 APR 2006